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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,792	11/16/2000	Mary Collins		3965

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,792	COLLINS ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,41,46-57,59-65,67-69,78-81 and 83-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,18,46-49,51,54-57,59,86,88 and 97-100* is/are allowed.

6)☒ Claim(s) *8,41,50,52,53,60-65,67-69,78-81,83-85,87, 89,96 and 101-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

1. Receipt of Applicants' arguments and amendments filed on 09 February 2004 is acknowledged. Claims 41, 46, 50-54, 60, 62, 68, 78, and 84 have been amended and new claims 86-104 have been added. Thus claims 18, 41, 46-57, 59-65, 67-69, 78-81 and 83-104 are pending and under consideration.

2. The following previous objections and rejections are withdrawn in light of Applicants amendment filed on 02/09/04:

(I) The rejection of claims 46-61 made under 35 U.S.C. 112, first paragraph, for not enabling an antibody that binds to "all" possible IL-13bc proteins, because these claims now recite specific SEQ ID Nos.

(II) The rejection of claims 18, 41, 50, 51, 52, 58,60, 68,74, 76, 78, 82 and 84 made under 35 U.S.C. 112, second paragraph, for reciting "modulating".

Response to Arguments:

Non-statutory double patenting rejection (obviousness-type)

3a. Claim 41, (and dependent claim 87) stand rejected and claims 53,61, 69, 85 and 96 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,248,714, for reasons of record, set forth in the office action mailed on 02/07/2003, page 4.

Claims 53, 69, 85 and 96, (like claim 41) are drawn to a method of inhibiting the binding of 1L-13 to 1L-13 receptor in a mammalian subject by administering a therapeutically effective amount of a composition comprising an antibody which specifically reacts with an isolated IL-13bc protein of SEQ ID No:4, or to an isolated IL- I

3bc or which comprises the amino acid sequence from amino acid 26 to 341 or 363 to 380 of SEQ ID NO:4.

Applicants argue that claim 1 of U.S. Patent No.6,248,714 relates to the use of soluble IL-13 receptor proteins to inhibit IL-13 function by binding to IL-13 protein. However, the instant invention is directed to antibodies that bind to IL-13. Applicants further argue that such antibodies can inhibit IL-13 function by binding to the receptor and thereby blocking access to IL-13 to bind to wild type receptor.
These arguments have been considered but are not deemed persuasive.

Claim 1 of U.S. Patent No. 6,248,7 14 is drawn to a method of inhibiting the binding of 1L- I 3 to IL-1 3 receptor in a mammalian subject by administering a therapeutically effective amount of a pharmaceutical composition comprising a protein of SEQ ID NO:4, or a protein which comprises the amino acid sequence from amino acid 26 to 341 or 363 to 380 of SEQ ID NO:4. Instant claims 41, 63, 61, 69, 85 and 96 are drawn to a method of inhibiting the binding of IL-13 to its receptor, by administering antibodies that bind to the IL-13 binding chain comprising the amino acid sequence set forth in SEQ ID NO:4 or which comprises the amino acid sequence from amino acid 26 to 341 or 363 to 380 of SEQ ID NO:4.

Instant specification describes the polypeptide of SEQ ID NO:4 as being the human IL-13 binding chain of the IL-13 receptor, (see page 6 , lines 12-20). Therefore, the administration of this peptide would inhibit the binding of the IL-13 to the native IL-13 receptor, because it would bind to IL-13. Likewise administration of antibodies that are directed to the polypeptide of SEQ ID NO:4 would also inhibit the binding of IL-13 to the

native receptor, because these antibodies would bind to IL-13 receptor. The novelty of the instant invention is the polypeptide of SEQ ID NO:4, therefore, whether the polypeptide itself is administered or whether antibodies that are directed against this polypeptide is administered, the same result would be achieved. Therefore, it would have been obvious to one skill in the art to use an antibody that binds to the binding chain portion of the IL-13 receptor to inhibit the binding of IL-13 to its receptor, because IL- 13 would not bind to its receptor in the absence of the IL-13 bc.

Claim rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. The rejection of claims 62-65, 67-69, 78-81, 83-85 stand rejected and new claims 89-96, 101, 102 and 103-104 are also rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office action mailed on 08/18/2003, pages 5-9.

Applicants argue that the specification describes how to determine whether a fragment of IL-13 bc binds IL-13, and that the biological activity possessed by the protein is the ability to bind IL-13 or a fragment and that the kD is about 10.1-100 nM. Applicants also argue that the specification clearly identifies the extracellular domain of IL-13 bc (amino acids 26-341) is involved in IL-13 binding. Applicants further argue that claim 78 is fully enabled, because the antibodies recited bind to IL-13 variants that are encoded by nucleic acid sequences which hybridize to the nucleotide of SEQ ID NO:3. thus, the scope is not infinite but is limited to antibodies that binds to IL-13 variants that

can in turn bind to IL-13. Applicants also argue that they have provided hybridization methods under highly stringent conditions. Finally, Applicants contend that it is well known in the art that antibodies could be raised against virtually any protein and the level of and knowledge in the art is high.

These arguments have been fully considered, but are not deemed persuasive.

Firstly, the issue is not whether the skilled artisan is able to determine whether a fragment binds to IL-13, but what is the predictability that "all" possible fragments of IL-13bc would bind to IL-13. A fragment can be as small as 3 amino acid residues, and as big as the extracellualr domain (amino acid resides 26-341), thus Applicants have not disclosed a representative number of fragments that display the desired activity. Therefore, the disclosure that one fragment (extracellular domain) may display the desired activity, is not sufficient to enable claims that encompass "all" possible fragments. Secondly, applicants have not disclosed one single variant of IL13bc, that binds to IL-13. The disclosure of hybridization method and conditions is not sufficient to enable claims that recite "variants", because the quantity of experimentation to determine which of the enormous number of nucleic acids that are capable of hybridizing to the nucleic acid of SEQ ID NO:3, would encode a variant of IL-13bc with the desired property, is undue. Finally, it is true that the level of skill in the relevant art is high, and that that antibodies could be raised against virtually any protein, however, the issue is whether the generated antibodies would have the desired activity. Applicants are providing an invitation for trial and error experimentation, in which one of

skill in the art would have no expectation that antibodies directed against "all" possible variants of IL-13bc would perform the desired function.

4b. Claims 62-65, 67-69, 78-81, 83-85 stand rejected and new claims 89-96 and 103-104 are also rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office action mailed on 08/18/2003, pages 6-9.

Applicants argue that instant specification clearly defines what is meant by "biologically active fragment", and that Examples 3-5 provide written description support to identify such fragments of IL-13bc. Applicants also argue that the specification discloses that the extraceulluar domain of IL-13 bc (amino acid residues 26-3410) is the domain that binds IL-13. Applicants also argue that a person skill in the art would not expect substantial variation among species encompassed in claim 78, because the highly stringent hybridization conditions set forth in the claim would yield structurally similar DNAs and consequently similar proteins. Thus a representative number of species is disclosed.

These arguments have been considered fully but are deemed unpersuasive. Examples 3-5 of the instant specification disclose binding assays, but provide no written description for "all' possible IL-13 bc fragments that are biologically active. Although these procedures can be followed to determine which fragments of IL-13bc might bind to IL-13, however, this is not sufficient to satisfy the written provision of the35 U.S.C. 112, for claims that recite biologically active fragment. Instant specification discloses only one fragment that displays the desired activity, namely the extraceulluar domain of IL-13 bc (amino acid residues 26-341) binds to IL-13, however, this limitation is not

recited in claims 62, 78 or 89. Furthermore, the disclosure of one single fragment is not sufficient to satisfy written description for claims that encompass "all" possible IL-13bc fragments that are biologically active. Finally, Applicants have not disclosed the structure of a single variant that hybridizes to nucleic acid of SEQ ID NO:3, that encodes a polypeptide that binds to IL-13. Applicants have not disclosed a representative number of DNA molecules that fall within the scope of the claimed invention.

New rejections:

Claim rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 50, 52, 60, 68, 84 and 95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating asthma or allergic conditions by administering said an antibody into a mammalian subject suffering from said disease, is not enabling for a method of treating immune complex diseases, lupus, nephritis, glomerulomnephritis, thyroidistis, Grave's disease or immune deficiencies in a mammalian subject by administering to said subject an antibody that binds to IL-3bc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Instant claims 50, 52, 60, 68, 84 and 95 are overly broad for reciting immune complex diseases, lupus, nephritis, glomerulomephritis, thyroiditis, Grave's disease or immune deficiencies, because instant specification does not establish a nexus between any of these diseases and IL-13bc or IL-13, therefore, antibodies that bind to IL-13bc would not be expected to treat these diseases. It is well known in the art that interleukin-13 (IL-13), is an important contributor to the inappropriate immune response that can lead to allergy and asthma. Instant specification states that IL-13bc could be used to treat IL-13 related conditions, such as immune complex diseases, including lupus, nephritis, glomerulomephritis, thyroiditis, Grave's disease , (see page 12, lines 16-30). However, the specification does not show that any of these diseases has been actually treated by administering antibodies of the instant invention. Furthermore, immune deficiency encompasses disparate diseases that have various causes, diseases that are not expected to be treatable by the same agent. For example, some immune deficiency diseases are relatively common, such as recurrent infections, while others are rare such as X-linked agammaglobulinemia (XLA), severe combined immunodeficiency (SCID) and acquired Immune deficiency syndrome (AIDS). Therefore, Applicants have not shown that the claimed antibody is effective in treating all of the diseases that occur due to immune deficiency.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples,

(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, the skilled artisan would not predict with any degree of expectation of success that antibodies against IL-13bc would effectively treat , lupus, nephritis, glomerulomephritis, thyroiditis, Grave's disease or "all" possible immune deficiency diseases. Furthermore, prior art is silent on a method of treating the above mentioned diseases, by administering antibodies to IL-13bc of SEQ ID NO:4, and Applicants fail to establish a link between these diseases and IL-13 or IL-13bc. Therefore, instant specification is only enabling for a method of treating asthma or allergic conditions by administering said an antibody into a mammalian subject suffering from said disease.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 50, 52, 78-81, 83-85, 101 and 102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claims 50 and 52 both depend from claim 46, however, these claims are of the same scope. Claim 50 is drawn to an antibody to be used in a method of treating or inhibiting IL-13 related conditions, and claim 52 is drawn to a method of treating or inhibiting IL-13 related conditions, therefore these claims are of the same scope.

5b. Claim 78 is rejected as vague and indefinite reciting ".... Which hybridizes under highly stringent conditions....", which is a conditional term and renders the claim

indefinite. This rejection could be obviated by supplying specific conditions supported by the specification, which Applicants consider to be "stringent".

Claims 79-81, 83-85 and 101-102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, so far as they depend on claim 78 for the limitations set forth directly above.

Conclusion:

6. Claims 18, 46, 47, 48, 49, 51, 54, 55, 56, 57, 59, 86, 88, 97, 98, 99, 100 are allowable.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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17 April 2004

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